DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 28 Jul 2010 has been entered.

This Office Action is responsive to Applicant's Amendment and Remarks, filed 28 Jul 2010, in which claims 11, 14, and 21 are amended to change the scope and breadth of the claim, new claim 27 is added, and claims 13 and 19 are canceled.

This application is the national stage entry of PCT/FR05/00739, filed 29 Mar 2005; and claims benefit of foreign priority document FRANCE 0403450, filed 01 Apr 2004, and foreign priority document FRANCE 0411201, filed 21 Oct 2004; currently English language translations of these foreign priority document have not been filed.

Claims 11, 12, 14-18, 20, 21, 26 and 27 are pending.

Rejections Withdrawn

Applicant's Amendment, filed 28 Jul 2010, with respect to claims 11-13, 15-21 and 26 rejected under 35 U.S.C. 103(a) as being unpatentable over Junco et al. (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, 69-73, of record) in view of Majid et al. (US Patent 5,070,081, issued 3 Dec 1991, of record) has been fully considered and is persuasive, as amended independent claim 11 requires the presence of water as a diffusion agent.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 28 Jul 2010, with respect to claims 11-21 and 26 rejected under 35 U.S.C. 103(a) as being unpatentable over Junco et al. (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, 69-73, of record) in view of Majid et al. (US Patent 5,070,081, issued 3 Dec 1991, of record) and Lieberman et al. (Pharmaceutical dosage forms-- disperse systems, 1998, Marcel Dekker, Inc., 2nd ed., p1-46, of record) has been fully considered and is persuasive, as amended independent claim 11 requires the presence of water as a diffusion agent.

This rejection has been **withdrawn**.

The following are new grounds of rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended Claims 11, 12, 14-18, 20, 21, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Friess et al. (WIPO Publication WO 03/043604, published 30 May 2003, provided by Applicant in IDS mailed 29 Sep 2006) in view of Van Hees 2002 (Journal of Inclusion Phenomena and Macrocyclic Chemistry, 2002, 44, p271-274, provided by Applicant on IDS filed 29 Sep 2006). As Friess et al. is not in English, the US Patent Application Publication 2005/0274671 A1 of the 371 national stage entry of Friess et al. is provided and referenced to as Friess et al. herein.

Friess et al. teaches a method for preparing compounds for interaction of an active substance hardly soluble in an aqueous medium with a porous support comprising (a) mixing the active substance generated by supercritical fluid and the specific amount of porous support; (b) carrying out a molecular diffusion step by contacting in static mode a supercritical fluid with the mixture obtained at step (a) for the time required to improve the dissolution in the aqueous medium of the mixture obtained

at step (a); (c) washing the interactive compound obtained at step (b) with a supercritical fluid flow; (d) recuperating the particles of the interactive compound thus formed (abstract). Friess et al. teaches the step (b) performed with stirring and in the presence of a diffusion agent, most advantageously water, added continuously or discontinuously (page 5, paragraphs 98-102). Friess et al. teaches the embodiment wherein the molecular diffusion step mixture contains a mass ratio of 25% of water (page 8, paragraph 186-187). Friess et al. teaches the porous support is any appropriate porous support that is soluble in an aqueous medium and is advantageously selected from cyclodextrins and a mixture thereof (page 4, paragraph 65). Friess et al. teaches the supercritical fluid is advantageously CO_2 (page 4, paragraph 66). Friess et al. teaches the active agent may be a pharmaceutical, cosmetic or nutraceutical active, and advantageously it is an active substance selected from the group consisting of anilide derivatives, epipodophyllotoxin derivatives, piroxicam, valeric acid, octanoic acid, lauric acid, and stearic acid (page 3, paragraph 50). Friess et al. teaches advantageously the pressure of the supercritical fluid is between 10 MPa and 40 MPa and the temperature is between 0 and 120°C (page 5, paragraph 104).

Friess et al. does not specifically teach the processes comprising the successive step d. carrying out a step which consists of adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex under atmospheric pressure in a semi-solid medium wherein said agent for interaction

with the complex is an acid or a base (instant claim 11). Friess et al. does not specifically teach species of said agent for interaction (instant claim 14 and 27).

Van Hees et al. 2002 is drawn to the field of preparation of drug-cyclodextrin inclusion compounds and teaches addition of ternary agents can be significant factors in the formation of said inclusion compounds (page 271, abstract). Van Hees et al. 2002 teaches preparing complexes of piroxicam and β-cyclodextrin using super-critical CO_2 ($SCCO_2$) (page 271, left column, lines 9-10), the inclusion compound of an active substance whose aqueous solubility is poor and a host molecule in a dense pressurized fluid. Van Hees et al. 2002 teaches the addition of agents for interaction with the complex such as L-lysine, an amino acid that is a base, and the non-preferred aqueous ammonium hydroxide solution (page 273, right column, lines 15-20), as well as the use of citric acid, a carboxylic acid (page 274, right column, line 2).

It would have been obvious to one of ordinary skill in the art the time of the invention to combine Friess et al. in view of Van Hees 2002. Both Friess et al. and Van Hees 2002 are drawn to preparing complexes of an active substance hardly soluble in an aqueous medium with a porous support. One of ordinary skill in the art would have been motivated to combine Friess et al. in view of Van Hees 2002 in order to use a known technique to improve similar methods in the same way by the addition of agents for interaction with the complex such as L-lysine or citric acid. One of ordinary skill in the art would have had a reasonable expectation of success to combine Friess et al. in view of Van Hees 2002 because both Friess et al. and Van Hees 2002 teach preparing complexes of piroxicam and β-cyclodextrin using super-critical CO_2. MPEP 2144.04

IV.C. provides that selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results and selection of any order of mixing ingredients is *prima facie* obvious. In the instant case Friess et al. teaches a step (a) mixing the active substance generated by supercritical fluid and the specific amount of porous support, and it would have been obvious to select any order of the prior art process steps in the absence of new or unexpected results.

Regarding the absence of new or unexpected results, the instant specification shows unexpected results for the embodiment of piroxicam, β-cyclodextrin and ammonia (examples 1 and 6 at pages 26 and 28-29) or piroxicam, β-cyclodextrin and arginine (page 31 and 34-35). However, Van Hees et al. 2002 teaches the results are dependent on the type of porous host molecule, type of active agent, and type of ternary acidic agent (page 274, spanning left column, paragraphs 3-4 to right column,

paragraph 1 and figure 7 at top of left column).

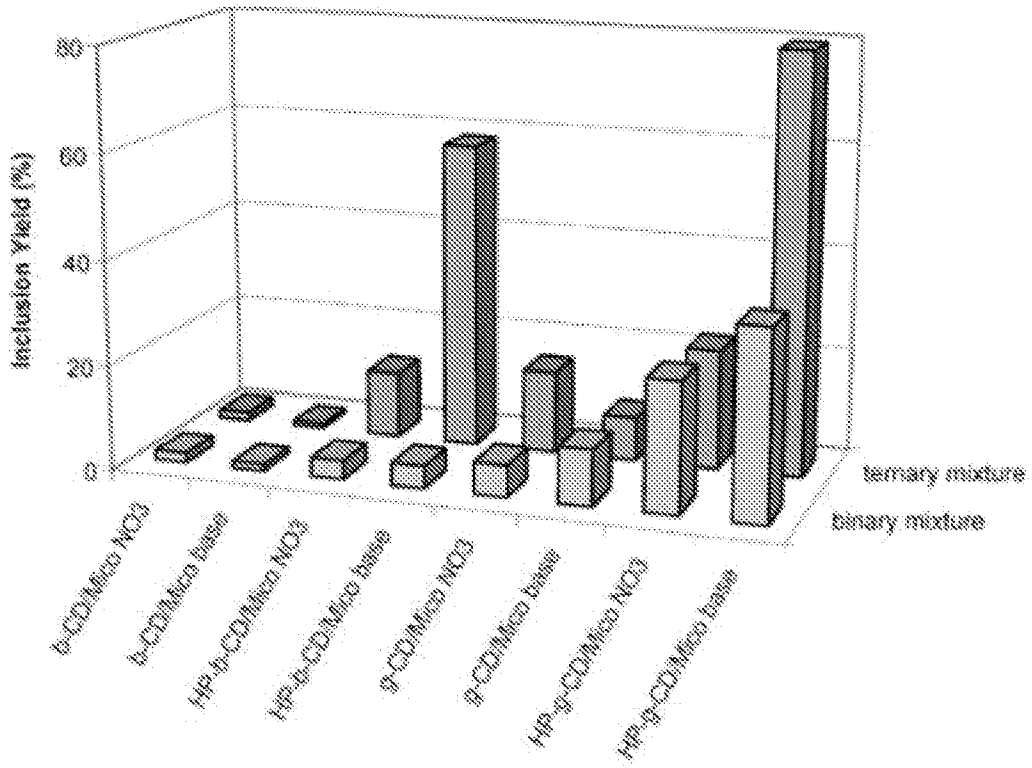

Figure 7. Influence of the type of CD, the type of miconazole and the addition of a ternary acidic agent on the inclusion yield using $SCCO_2$.

For example, in figure 7 the inclusion yield for γ-CD with miconazole nitrate increases for the mixture with the ternary acidic agent compared to the binary mixture, however the inclusion yield for γ-CD with miconazole appears to be the comparable for both binary and ternary mixtures or possibly greater for the binary mixture compared to the ternary mixture; conversely the inclusion yield for HP-γ-CD with miconazole nitrate appears to be the comparable for both binary and ternary mixtures or possibly greater for the binary mixture compared to the ternary mixture whereas the inclusion yield for HP-γ-CD with miconazole increases significantly for the mixture with the ternary acidic

agent compared to the binary mixture. MPEP 716.02(d) provides that the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." In the instant case Van Hees et al. 2002 suggests there is "no adequate basis for reasonably concluding that the great number and variety of compositions included in the claims would behave in the same manner as the tested composition.", therefore the evidence of unexpected results provided in the instant specification is not found to be commensurate in scope with the claims.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is (571)270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jonathan Lau
Patent Examiner
Art Unit 1623

/SHAOJIA ANNA JIANG/
Supervisory Patent Examiner
Art Unit 1623